

12/20/02

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Gary E. Borodic, M.D.)	Art Unit: 1644
Serial No.	:	09/382,837)	
Filed	:	August 25, 1999)	
For	:	Chemodenervating Pharmaceutical As Anti-Inflammatory Agent)	
Examiner	:	G.R. Ewoldt, Ph.D.)	

Declaration of Dr. Martin Acquadro

**VIA FACSIMILE
(703) 305-3014
ATTN: G.R. Ewoldt, Ph.D.**

Asst. Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Martin Acquadro, M.D., D.M.D., declare and state as follows:

1. I received my B.A. from Boston University, after which I received both my D.M.D. in 1980 and my M.D. in 1983 from Boston University. I trained in Internal Medicine at the Carney Hospital from 1983 to 1985 and then completed both a residency in Anesthesia and a Pain Management Fellowship at the Massachusetts General Hospital. I further ran a Pain Clinic in addition to practicing Anesthesia at the Massachusetts Eye and

Ear Infirmary for ten years before joining the MGH Pain Center in October of 1999. Presently, I am the Director of the Cancer Pain Program at the MGH Pain Center.

2. I have extensive experience in applications of Botulinum Toxin, cancer pain, and head and neck pain.
3. I am thoroughly familiar with the subject application, the Office Action Summary mailed on August 26, 2002, and with the prior art cited in the Notice of References cited.
4. As an expert in the field of the treatment of inflammation and pain, I am very familiar with the usage of concepts and terminology by those of ordinary skill in that field of endeavor, and how such practitioners of ordinary skill in that field of endeavor would have understood the concepts and terminology of the specification of the pending patent application as of the earliest priority date of the pending application, August 25, 1998.
5. One of ordinary skill in the art would clearly understand that one of the major thrusts of the specification is the use of botulinum toxin for treatment of neurogenic inflammation and that the physiological processes that the application's specification discloses as being affected by botulinum toxin are what constitute neurogenic inflammation as of the earliest priority date of the pending application, August 25, 1998.
6. One of ordinary skill in the art would understand that the invention encompasses a method of treating neurogenic inflammation when reading that the specification of mast cell and nerve cell release of "preformed mediators" and the blockage of such release by chemodenervating pharmaceuticals, such as botulinum toxin, would be clearly understood by one of ordinary skill in the art as referring to neurogenic inflammation and neurogenic mediators, and as indicating that the inventor had the invention as claimed in claims 17-19, and 21-23 in his possession

as of the earliest priority date of the pending application, August 25, 1998.

7. One of ordinary skill in the art, as of the earliest priority date of the pending application, August 25, 1998, would understand that the invention encompasses a method of treating neurogenic inflammation when reading the "Summary of Invention" section of the application that discloses "this new bioeffect of anti-inflammatory action is explained by the resultant blockage of mast and nerve cell release of histamine and other preformed mediators which result in vascular dilation *[sic]*, increased permeability, altered sensory experience, edema and erythema." ("Summary of Invention", paragraph 3).
8. Additionally, one of ordinary skill in the art, as of the earliest priority date of the pending application, August 25, 1998, would understand that the invention encompasses the treatment of neurogenic inflammation and the antagonism of at least one neurogenic mediator when reading the following disclosures: "[C]hemodenervative pharmaceuticals such as botulinum toxin...are effective anti-inflammatory agents" ("Summary of Invention", paragraph 2); "The subject anti-inflammatory agent's unique property relates to the suppression of the component for the inflammatory response which occurs rapidly, and which is mediated by neural reflex mechanisms" ("Summary of Invention", paragraph 6).
9. The phrase "[I]nflammation in torticollis in peripheral tissues may be neurogenically mediated", also indicates that the Applicant is specifically disclosing a method comprising a neurogenic process as of the earliest priority date of the pending application, August 25, 1998. ("Spasmodic Torticollis", paragraph 3).
10. The present patent application was filed on August 25, 1999. While the Examiner is correct in stating that U.S. Patent No.

6,063,768 was not issued until after the present application's filing date, the '768 patent was filed on September 4, 1997 and is a continuation-in-part of a September 6, 1996 provisional application. Thus, the '768 patent shows the understanding that one of ordinary skill in the art would have during this time period. The Applicant does not appear to claim that "what is disclosed in the '768 patent must therefore be considered to be disclosed in the instant application", as the Examiner argued. (Office Action mailed August 26, 2002, p.5). Rather, the Applicant merely appears to be directing the Examiner's attention to the '768 patent to show similar language pertaining to the treatment of neurogenic inflammation with botulinum toxins during a similar time period. Again, this is a clear example of how one of ordinary skill in the art would have understood the disclosures of the treatment of neurogenic inflammation in the present specification as of the earliest priority date of the pending application, August 25, 1998. (Amendment After Final Office Action dated March 26, 2002; p. 7).

11. The '768 patent specifically states that "cells that release neuropeptides and other mediators, activators or promoters of inflammation such as sensory and autonomic neurons and other secretory cells play a role in inflammation" and that "botulinum toxins block the actions of these mediators." ('768 patent, Col. 1, lines 24-29). In the same regard, the present application discloses, as of the earliest priority date of the pending application, August 25, 1998, that "this new bioeffect of anti-inflammatory action is explained by the resultant blockade of mast and nerve cell release of histamine and other preformed mediators which result in vascular dialation [*sic*], increased permeability, altered sensory experience, edema and erythema. It is thus a finding of this invention that inflammation is inhibited by administration of the

subject chemodenervative agent." ("Summary of Invention", paragraph 3).

12. Furthermore, the paper entitled "Histamine and Tumor Necrosis Factor-alpha Production From Purified Rat Brain Mast Cells Mediated by Substance P", which was cited by the Applicant, discloses the role played by substance P in triggering neurogenic inflammation. It should be clear that the present application's disclosure would be understood to include that "chemodenervative pharmaceuticals such as botulinum toxins may be used to successfully treat neurogenic inflammation" as of the earliest priority date of the pending application, August 25, 1998. (Amendment After Final Office Action dated March 26, 2002; p. 9-10).
13. Additionally, as previously explained by the Applicant, Sann et al. and McDonald et al., which were published in 1996, disclose the understanding and meaning of "neurogenic inflammation." (Amendment After Final Office Action dated March 26, 2002; p. 8). Both of these characterizations are consistent with the '786 patent's explanation and the disclosure within the present invention pertaining to the treatment of neurogenic inflammation. Once again, demonstrating as of the earliest priority date of the pending patent application, one of ordinary skill would have understood the disclosure to include the treatment of neurogenic inflammation with botulinum toxins as of the earliest priority date of the pending application, August 25, 1998.
14. Based on the references mentioned herein (numbers 11-14), it is clear that one of ordinary skill in the art would understand the present application's disclosure to indicate the inclusion of the treatment of neurogenic inflammation as particularly claimed in claims 17-23 as of the earliest priority date of the pending application, August 25, 1998.

15. The specification provides a number of working examples of treating inflammation with a chemodenervative pharmaceutical, such as botulinum toxin, without causing muscle weakness, and with doses within the claimed range. The specification specifically states that "botulinum toxin injected into red areas noted to be painful and thermally active in accordance with the subject invention has been demonstrated to block the erythema, pain, increased tenderness, and heat loss within the area", and that "minimum doses [for achieving this effect] range between 0.6 units to 15 units and are far lower than that required to produce regional weakness". ("Spasmodic Torticollis", paragraph 4). As explained throughout the specification, and as well-understood by one of ordinary skill in the art, redness (erythema), pain, increased tenderness, and heat loss are some of the cardinal defining characteristics of inflammation. Additionally, the specification discloses an "inject[ion] with .675 mouse units of botulinum toxin". ("Conjunctivitis", paragraph 3). Thus, one of ordinary skill in the art finds ample support in the specification for successfully treating inflammation with a chemodenervating agent, such as botulinum toxin, with a dose less than 2.5 units and without causing muscle weakness as of the earliest priority date of the pending application, August 25, 1998.
16. The first paragraph of the "Background of the Invention" section of the specification, applicant explicitly refers to inflammation as involving "complement, arachidonic acid metabolites such as prostaglandin and leukotrienes, cytokines, preformed mediators such as serotonin and histamine, and enzymes." One of ordinary skill in the art would understand that the term cytokine is defined in the art as referring to interleukin-1, interleukin-2, and tumor necrosis factor, and that 5-hydroxytryptamine is a synonym for

serotonin as of the earliest priority date of the pending application, August 25, 1998.

17. In the first paragraph of the "Summary of the Invention", applicant explicitly states that "low dosages of the subject chemodenervative agent reduces histamine release and releases of other preformed mediators associated with mast cell degranulation." In the second and third paragraphs of the "Mast Cells" section of the specification, applicant explicitly refers to "preformed mediators such as histamine, newly formed mediators such as leukotrienes and prostaglandins, cytokines, including interleukin-5, interleukin-8, kininogenase, and platelet activating factor", as well as "tumor necrosis factor alpha" and "substance P". Thus, support for the terms "substance P", "interleukins", "tumor necrosis factor", and "serotonin" are explicitly found in the specification and would be understood by one of ordinary skill in the art as of the earliest priority date of the pending application, August 25, 1998.
18. With regard to the other terms recited in claim 19, one of ordinary skill in the relevant art would clearly understand that applicant's explicit references in the specification to "preformed mediators", "cytokines", and "newly-formed mediators" encompasses all of the specific neurogenic inflammatory mediators enumerated in claim 19, and thus indicates that applicant was in possession of the invention in every particular as claimed in claim 19 as of the earliest priority date of the pending application, August 25, 1998.
19. It is well understood by those of ordinary skill in the art that gout is a disease that is most fundamentally characterized by inflammatory response in the joints. Thus, one of ordinary skill in the relevant art would clearly conclude from applicant's statements in the specification regarding treatment of joint inflammation with chemodenervating pharmaceuticals that applicant was in possession of the invention as claimed in claim 22—including

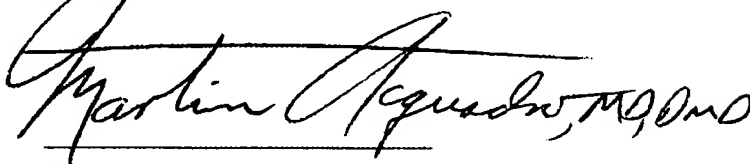
specifically the treatment of neurogenic inflammation caused by gout—as of the earliest priority date of the pending application, August 25, 1998.

20. Applicant discloses in numerous places in the specification that it is within the scope of the invention to reduce inflammation by inhibiting histamine. For example, in the first paragraph of the “Summary of the Invention”, applicant explicitly states that “low dosages of the subject chemodenervative agent *reduces histamine release*” (emphasis added). Claim 15 recites “botulinum toxin immunotypes which block mast cell release of histamine”. Furthermore, in the various examples disclosed later in the specification, such as successful treatment with chemodenervative pharmaceuticals of cholinergic urticaria, treatment of blepharoconjunctivitis, etc., it is well known in the relevant art that those disorders are always associated with increased histamine activity in the affected tissues, and that increased histamine activity is a major cause of the inflammation. It would thus be clear to one of skill in the relevant art that applicant was in possession of the invention as claimed in claim 23—including the treatment of neurogenic inflammation by inhibiting histamine—as of the earliest priority date of the pending application, August 25, 1998.

21. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 12/19/2002

Respectfully submitted,

A handwritten signature in black ink, reading "Martin Acquadro, M.D., D.M.D.", written over a horizontal line.

Martin Acquadro, M.D., D.M.D.

CURRICULUM VITAE

Date Prepared: 12/19/2002

Name: Martin Andrew Acquadro
Address: 93 Emerson Road, Wellesley, Massachusetts 02481-3411
Date of Birth: May 21, 1954
Place of Birth: Boston, Massachusetts, United States of America

Education:

Year	Degree	Institution
1975	B.A.	Boston University Chemistry (Major Field of Study) Economics (Major Field of Study)
1980	D.M.D	Boston University Goldman School of Graduate Dentistry Dental Medicine
1983	M.D.	Boston University School of Medicine

Postdoctoral Training:

Year	Specialty	Place of Training
1983-1984	Internal Medicine	Carney Hospital, Boston, MA (Intern)
1984-1985	Internal Medicine	Carney Hospital, Boston, MA (Resident)
1986-1988	Anesthesiology Pain Medicine	Massachusetts General Hospital, Boston MA (Resident) 1988 Massachusetts General Hospital, Boston, MA (Fellow)

Licensure and Certification:

Licenses:

Dental Medicine

1980 Commonwealth of Massachusetts Reg. No. 14398
1980 Commonwealth of Pennsylvania Cert. No. DS- 021901-L

Medicine

1984 Commonwealth of Pennsylvania Cert. No. MD-032796-E
1985 Commonwealth of Massachusetts Reg. No. 54006

Certifications:

Dental Medicine

1979 American Dental Association - Certified
National Board Dental Examinations
1980 Northeast Regional Board of Dental Examiners - Certified
Certificate issued.

Medicine

1984 Diplomate, National Board of Medical Examiners
Cert. No. 239440
1989 Diplomate, American Board of Anesthesiology
Cert. No. 16985
1990 Diplomate, American Academy of Pain Management
Cert. No. 1169
1990 Diplomate, American Board of Internal Medicine
Candidate No. 113745
1993 Fellow, American College of Pain Medicine
Certificate issued.
1994 Diplomate, American Board of Pain Medicine
Certificate issued.
1996 Fellow, American College of Physicians
Certificate issued.
1998 Certificate in Pain Management, American Board of Anesthesiology
Certificate issued.

Chemistry

1975 American Chemical Society's Criteria for
Professional Education - Certified Major
Field of Study - Chemistry. Certificate issued.

Aviation

1972 Private Pilot Certification No. 2175581
Federal Aviation Administration
1995 Instrument Rating
Federal Aviation Administration

Academic Appointments:

Year	Academic Title	Institution
1974	Teaching Assistant in Chemistry Inorganic and Organic- Lab and Problem Solving.	Boston University
1975	Teaching Assistant in Chemistry Organic-Lab and Problem Solving.	Boston University
1975	Teaching Assistant in Nurse Science Chemistry Lab and Problem Solving.	Boston University
1986-1988	Clinical Fellow in Anaesthesia	Harvard Medical School

1988-1997	Clinical Instructor in Anaesthesia	Harvard Medical School
1997-present	Assistant Professor, Anaesthesia	Harvard Medical School

Hospital Appointments:

Year	Hospital Title	Hospital
1986	Affiliate Staff in Medicine	Carney Hospital, Boston, MA
1988-1989	Assistant in Anesthesia	MEEI, Boston, MA
1989-1995	Assistant Anesthesiologist	MEEI, Boston, MA
1995-1999	Associate Anesthesiologist	MEEI, Boston, MA
1999-present	Associate Staff, Otolaryngology	MEEI, Boston, MA
1999-present	Assistant Anesthetist	Mass. Gen. Hosp., Boston, MA

Other Professional Positions and Major Visiting Appointments:

1994	Visiting Professor, Department of Human Anatomy and Surgical Anatomy, Laval University, Faculty of Medicine, Quebec, Canada G1K 7P4.
1995	Visiting Professor, Department of Human Anatomy and Surgical Anatomy, Laval University, Faculty of Medicine, Quebec, Canada G1K 7P4.

Awards and Honors:

Various awards achieved in competition for instrumental and composition, piano, while engaged in extramural formal study of the piano, primary and secondary schools.

1974	'Excellence' for course work and research in Physical Chemistry III. Research Title: 'Binding and Solubility of Acetophenone to Bile Salt Micelles as Determined by H NMR Spectroscopy.
1977	Honored by invitation as guest speaker before the economists at Chase Manhattan Symposium, New York, NY and before the U.S. House Subcommittee on Social

Security concerning my research, 'Contributory Pension as an Effective Economic Tool', and 'High Interest Rates: The Paradoxical Misfire.'

- 1980 Appointed Member of the Alumni Board for the Mason Memorial Fund, Dr. Norman Lichtin, Chairperson, Department of Chemistry, Boston University.
- 1980 National Student Service Award Winner, Phi Delta Epsilon Medical Fraternity.
- 1980 Appellation, Past Undergraduate Regional Coordinator Phi Delta Epsilon Medical Fraternity.
- 1981 Honors, Surgical Clerkship, University Hospital, Boston University School of Medicine.
- 1981 Awarded 'Excellence' for an optional essay, Dr. Barry Make, Pulmonary Section, Biology of Disease, Second year, Boston University School of Medicine
- 1982 Extraordinary Leadership Award, Boston University School of Medicine Chapter, Phi Delta Epsilon Medical Fraternity.
- 1982 Co-Chairperson, Phi Delta Epsilon Medical Fraternity, 1982 International Scientific Convention, Boston, MA.
- 1983 Past Master, Wellesley Masonic Lodge, Wellesley, MA.
- 1983 Received 'Honors Evaluation' in eight out of ten Fourth Year Elective Rotations, Boston University School of Medicine.
- 1984 Achievement Award, Scientific Paper with Excellence, 'Presentation of Papers Evening', The Carney Hospital. Title: 'Erythema Multiforme.'
- 1984 Achievement Award, Scientific Paper with Excellence, 'Presentation of Papers Evening' The Carney Hospital. Title: 'Radionucleide Cisternograms and the Question of Normal Pressure Hydrocephalus -- A Reappraisal'.
- 1993 Fellow, American College of Pain Medicine.
- 1996 Fellow, American College of Physicians.

Major Committee Assignments:

National and Regional:

1989-1990 Massachusetts Peer Review Organization, Waltham, MA

University:

1990- 1996 Member, Boston University, Department of Chemistry, Alumni Board.

Hospital:

1988-1990 Education Committee, Department of Anesthesia
Massachusetts Eye and Ear Infirmary, Boston, MA
1990-1999 Chairman, Education Committee, Department of Anesthesia
Massachusetts Eye and Ear Infirmary, Boston, MA
1989-1999 Chairman, Respiratory Care Committee, MEEI
1989-1990 Anesthesia Quality Assurance Committee, MEEI
1989-1995 Long Range Planning Head and Neck Committee, MEEI
1989-1990 Member, Hospital Based Services Committee, MEEI
1989-1990 Member, Task Force on Ambulatory Surgery, MEEI
1992-1995 Member, Intermediate Care Unit Committee, MEEI
1990-1995 Representative, MEEI and Physician Staff, Inc. (MeSH)
1990-1991 Member, By-Laws Committee, MEEI
1990-1991 Member, Patient Relations Program, MEEI
1999-1999 Chairman, CQI Committee, Anesthesiology, MEEI.

Memberships, Offices, and Committee Assignments in Professional Societies:

Membership Summary:

1973-1995 American Chemical Society
1973-1995 American Chemical Society, Northeast Section
1976-1996 American Economic Association
1982-1995, 1999-Present Massachusetts Medical Society
1982-1995 Suffolk District Medical Society
1982-1995, 1999-Present American Medical Association

1983-Present Society of American Value Engineers
1983-Present Society of American Value Engineers, Paul Revere Chapter
1985-Present American College of Physicians
1986-1995, 1999-Present Massachusetts Society of Anesthesiologists
1987-1995, 1999-Present American Society of Anesthesiologists
1987-1995 New England Society of Anesthesiologists
1990-1995 American Academy of Pain Management
1993-Present American Academy of Pain Medicine
1993-Present American Pain Society
1993-Present New England Pain Society
1993-1995 American College of Pain Medicine (merged into Amer. Acad. Pain Med.)
1993-1995 International Association for the Study of Pain
1994-1995 National Headache Foundation

1978-Present	Member, Executive Committee, Phi Delta Epsilon Medical Fraternity.
1980-1983	Member, Scientific Convention Committee, Phi Delta Epsilon Medical
1982	Co-Chairman, Boston Scientific Convention, Phi Delta Epsilon Medical Fraternity.
1983-Present	Member, Economic Development Committee, Phi Delta Epsilon Medical Fraternity.
1989-1992	Member, Board of Directors, Engineering Societies of New England
1992-1995	President, Paul Revere Chapter, Society of American Value Engineers
1994-Present	Member, Finance and Budget Committee, Phi Delta Epsilon Medical Fraternity.
1988-1992 & 1995-Present	Member, Board of Directors, Paul Revere Chapter, Society of American Value Engineers
1995-1998	Treasurer, The Foundation of the Phi Delta Epsilon Medical Fraternity.
1993	Fellow, American College of Pain Medicine
1996	Fellow, American College of Physicians

Editorial Boards:

1993-1997	Associate Editor, Phi Delta Epsilon News and Scientific Journal, Phi Delta Epsilon Medical Fraternity. 1898 East Southern Ave., Tempe, AZ 85282
1993	Reviewer, Anesthesiology
1993	Reviewer, Journal of Clinical Anesthesia.

Major Research Interests:

1. Determinants of Headache and Associated Functional Disability after Acoustic Neuroma Surgery.
2. Prospective, Double-Blind, Placebo-Controlled, Randomized Study of Treatment of Myofascial Pain with Botulinum Toxin in Postoperative Acoustic Neuroma Patients.
3. Prospective, Double-Blind, Placebo-Controlled, Randomized Study of the Effects of Saline or Local Anesthetic Injections for Patients with Nociceptive Dizziness.
4. Treatment of Chronic Paranasal Sinus Pain with Minimal Sinus Pathology.

Please refer to the Bibliography Section for other research interests.

Principal Clinical and Hospital Service Responsibilities:

1989-Present	Director, Diagnostic and Therapeutic Pain Management Unit, MEEI
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Major Administrative Responsibilities:

1989-1999	Chairman, Respiratory Care Committee, MEEI
1990-1999	Director, Education, Dept. of Anesthesia, MEEI
1999-1999	Chairman, CQI, Anesthesiology, MEEI

Self Report of Teaching:

1974-1975	Taught Inorganic and General Chemistry to Boston University Students.
1975	Taught Nursing Science Chemistry to Boston University Students.

1983-1985

Taught Boston University Medical Students at Carney Hospital.

Leadership Roles:

1988-1990 - as Staff Member; then,

1989-1999 - as Chairman of MEEI Respiratory Care, then,

1990-1999 - as Director of Education, Dept of Anesthesia, MEEI, and

1990-1999 - as Director, Diagnostic and Therapeutic Pain Management Unit:

Teaching Harvard Medical Students, Massachusetts General Hospital

Residents and Fellows in Anesthesiology, Pain, Pediatrics, and Pediatric Intensive Care,

Harvard Dental Students, University of Massachusetts Medical School Anesthesiology

Residents, and St. Elizabeth Hospital Anesthesiology Residents in Clinical

Anesthesiology.

Responsibilities include the development and maintenance of manuals, syllabi, references, teaching materials, in-service examinations, and evaluation instruments of trainees and staff. Responsibilities also include Department Staff Education, including Journal Club, Staff In-service Annual Exam of Journal Club Articles, and direction and production of the Department Morbidity and Mortality Rounds, along with other Staff Department Teaching. Also, as Chairman of Respiratory Care, responsible for Hospital Staff and Hospital Nursing Staff coordination of in-service updates and continuing quality improvement on issues relevant to respiratory care.

1999-Present Massachusetts General Hospital, Department of Anesthesia and Critical Care, and the Massachusetts General Hospital Pain Center: Teaching MGH Fellows and Residents.

1990

Co-Director of an 8 hour seminar on Value

1991

Engineering/Management for Paul Revere Chapter,
Society of American Value Engineers.

1992

Co-Director: Anesthetic Management For Otorhinolaryngologic And
Ophthalmic Surgery. Sponsored by Harvard Medical Education, and
Massachusetts Eye & Ear Infirmary, Department of Anesthesiology.

1993

Visiting Professor, Department of Human Anatomy and Surgical
Anatomy, Laval University, Faculty of Medicine, Quebec, Canada
G1K 7P4.

1994

Visiting Professor, Department of Human Anatomy and Surgical
Anatomy, Laval University, Faculty of Medicine, Quebec, Canada
G1K 7P4.

1995

Course Director: Sinus Pain Treatment Sponsored by the Department of
Anesthesia, MEEI and The New England Pain Association.

2000

Visiting Professor, Department of Anesthesiology, University of British Columbia
and Vancouver General Hospital.

2000

Visiting Professor, Department of Human Anatomy and Surgical Anatomy, Laval

Lectures:

International

1. Sept. 1, 1993 Chronic Pain: Focus on Neuropathic Pain. McGill University School of Medicine, Montreal, Canada. Sponsored by Phi Delta Epsilon Medical Fraternity.
2. Sept. 1, 1993 Specialty of Anesthesiology. McGill University School of Medicine, Montreal, Canada. Sponsored by Phi Delta Epsilon Medical Fraternity.
3. Jul. 6, 1994 Anesthesia for Ophthalmic Surgery. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
4. Jul. 7, 1994 Chronic and Neuropathic Pain. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
5. Jul. 7, 1994 Airway Management: Focus on Intubation. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
6. Oct. 1, 1994 American Medicine: Early 1900's to the Present. McGill University School of Medicine, Montreal, Canada. Sponsored by Phi Delta Epsilon Medical Fraternity.
7. Aug. 9, 1995 Anesthesia for Ophthalmic Surgery. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
8. Aug. 10, 1995 Chronic and Neuropathic Pain. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
9. Aug. 11, 1995 Airway Management: Focus on Intubation. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
10. Sept. 30, 1995 Airway Management. McGill University School of Medicine, Montreal, Canada. Sponsored by Phi Delta Epsilon Medical Fraternity.
11. Mar. 8, 2000 Neuropathic Pain. Visiting Professor. University of British Columbia School of Medicine, Department of Anesthesia, Vancouver General Hospital, Vancouver,

British Columbia, Canada. Coordinator: Dr. Ken Turnbull.

12. Mar. 8, 2000 Visiting Professor Resource. Didactic Seminar, Department of Anesthesia, Royal Columbian Hospital, Resident and Fellow Education, University of British Columbia, Vancouver, British Columbia, Canada. Coordinator: Dr. Ken Turnbull.
13. Mar. 8, 2000 Neuropathic Pain. Guest Lecturer. Simon Fraser University. Phi Delta Epsilon Medical Fraternity, Vancouver, British Columbia, Canada. Coordinator: Neil Tran.
14. Mar. 8, 2000 Current Concepts in Pain. Visiting Professor. University of British Columbia School of Medicine, Department of Anesthesia, Vancouver General Hospital, Vancouver, British Columbia, Canada. Coordinator: Dr. Ken Turnbull.
15. Mar. 9, 2000 Current Concepts in Pain. Grand Rounds. Royal Columbian Hospital. Vancouver, British Columbia, Canada. Coordinator: Dr. Peter Scoates.
16. Aug 14, 2000 Nociceptive and Neuropathic Pain. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
17. Aug 14, 2000 Airway Management: Focus on Intubation. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
18. Aug 15, 2000 Spinal and Epidural Anesthesia. Visiting Professor. Laval University School of Medicine, Quebec City, Quebec, Canada. Anatomy Course Director: Professeur Miodrag S. Jovanovic, DABS, FRCS(C), FICS.
19. June 9, 2002 Application of botulinum toxin in multiple pain syndromes of the head and neck region. International Conference 2002: Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hanover, Germany, June 8 – 11, 2002, Hans Bilgalke, Course Coordinator.
20. June 9, 2002 Sensory nerve adaptation, pain management, and application of botulinum toxin in a tertiary care pain center. International Conference 2002: Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hanover, Germany, June 8 – 11, 2002, Hans Bilgalke, Course Coordinator.

National

1. Jul. 19, 1991 The Epidural Catheter for Perioperative Pain Management. Videotaped lecture for Abbott Laboratories.
2. Oct. 18, 1991 Acute and Chronic Pain Management: Emphasis on Pediatrics. For 22nd Annual Seminar, 'Children as Patients: Evolving Issues', by the Rhode Island Society of Hospital Pharmacists.
3. Apr. 24, 1993 Approach to Chronic Head, Neck, and Ocular Pain. Third Annual Symposium, University of Connecticut, Farmington, CT. Sponsored by the Connecticut Chronic Pain Outreach Network.

4. Oct. 2, 1993 Medicine at the Crossroads: Medical Ethics and Genetics. Cornell Medical School, New York, NY. Sponsored by Phi Delta Epsilon Medical Fraternity.
5. Oct. 2, 1993 Parental Choices and Modern Genetics. (Panel speaker and moderator.) Cornell Medical School, New York, NY. Sponsored by Phi Delta Epsilon Medical Fraternity.
6. Feb. 16, 1995 Orofacial Pains. American Academy of Pain Medicine, 1995 Review Course in Pain Medicine. Edward C. Covington, MD, Chair, Review Course, Palm Springs, CA.
7. Aug. 25-26, 1998 Symposium on Botulinum Toxin. University of Vermont School of Medicine, Departments of Neurology and Neurophysiology. Director: Dr. Gary Borodic.

Regional

1. Jul. 23, 1988 Anesthesia for Recovery Room Nurses. Choate-Symmes Hospitals, Continuing Education Seminar.
2. Feb. 28, 1990 Anesthesia and its Effects on Respiratory Function. Dept. Of Respiratory Therapy, Massachusetts General Hospital.
3. Jan. 11, 1991 Medicine and Its Chemical Weave. Department of Chemistry, Boston University.
4. Jul. 16, 1991 Diagnostic and Therapeutic Pain Management: Focus on Acute and Chronic Pain for the ENT and Eye Patient. Headache Center, Faulkner Hospital.
5. Jul. 31, 1991 Anatomy and Physiology of the Epidural Space, and Epidural Pain Management. Abbott Laboratories, Hospital Products Division, Vista International Hotel, Waltham, MA.
6. Oct. 5, 1991 Approach to Comprehensive Pain Management. Harvard Continuing Medical Education Course: Anesthetic Management for Otorhinolaryngologic and Ophthalmic Surgery.
7. Sept. 21, 1992 Anesthesia for Open Eye Injuries. Anesthesia Grand Rounds, Tufts New England Medical Center.
8. Mar. 4, 1993 Anesthetic Management and Open Eye Injuries. Anesthesia Grand Rounds Case Discussion, Massachusetts General Hospital.
9. Mar. 18, 1993 Selected Topics in Anesthesiology Concerning Ophthalmic Patients Harvard Continuing Medical Education Course, 'Intensive Review of Ophthalmology'. Course Directors: D. Miller, MD, F. Jakobiec, MD.
10. May 13, 1993 Anesthetic Pain Management in the Multidisciplinary Approach to Chronic Facial Pain. Sponsored by the New England Pain Association. Spaulding Hospital. Course Coordinator: Raymond Maciewicz, MD, PhD.
11. Nov. 21, 1993 Pain Management of Myofascial Pain. Lahey Clinic Medical Center, Burlington, MA. Sponsored by the National Spasmodic Torticollis Association. Coordinator: Ann

Lebrun.

12. Mar. 26, 1994 Comprehensive Approach to Pain in the Torticollis Patient. Kent County Hospital, Warwick, RI. Sponsored by the National Spasmodic Torticollis Association. Coordinator: Denise M. Dufault.
13. Apr. 9, 1994 Anesthesia for Ophthalmic Surgery. Harvard Continuing Medical Education Course, 'Intensive Review of Ophthalmology'. Course Directors: D Miller, MD, F. Jakobiec, MD.
14. Apr. 9, 1994 Paranasal Sinus, Head, and Facial Pain. Harvard Continuing Medical Education Course, 'Sinus and Trans-Sinus Surgery: Traditional and Endoscopic'. Course Directors: Salah Salman, MD, and William Montgomery, MD.
15. Apr. 9, 1994 Sinus Cripple. Harvard Continuing Medical Education Course, 'Sinus and Trans-Sinus Surgery: Traditional and Endoscopic'. Panel participant with case presentations. Course Directors: Salah Salman, MD, and William Montgomery, MD.
16. Oct. 12, 1994 An Anesthesiologist's Approach to Chronic Pain Management. Tufts Craniomandibular Disorder/Orofacial Pain Alumni Society, Park Plaza Hotel, Boston, MA. Director: Dr. Mehta, New England Medical Center.
17. Apr. 10, 1995 Emergency Medicine, Anesthesia: Problem Solving. Harvard Continuing Medical Education Course, 'Intensive Review of Ophthalmology'. Course Directors: Jakobiec FA, Miller D, and Weiter JJ.
18. Jun. 1, 1996 Controversies in Pain Management. Sphenopalatine Ganglion Blockade. At The John R. Graham Headache and Pain Center. Sponsored by The New England Pain Association and The John R. Graham Center at the Faulkner Hospital, Boston MA. Course Director: Graham Spruiell, MD.
19. Oct. 9, 1996 Clinical Update on the Neurophysiology of Head Pain. Gelb Pain Center, Tufts University School of Dental Medicine. Coordinator: Raymond Maciewicz, MD, PhD.
20. Nov. 1, 1996 Chronic Facial Pain: Evaluation and Therapy. The 1996 Gelb Symposium, Sponsored by The Gelb Pain Center of Tufts University School of Dental Medicine and The New England Pain Association. Course Director: Noshir Mehta.
21. Dec. 14, 1996 Sinus Pain Treatment. Sponsored by the Department of Anesthesia, MEEI and The New England Pain Association. Course Director: Dr. Martin A. Acquadro.
22. May 16, 2000 Current Concepts on Neuropathic Pain. Spaulding Rehabilitation Hospital, Boston, MA Course Director, Pat McAlary.

Hospital - Approximately four to six hospital lectures per year.

1. Jan. 24, 1989 Perioperative Considerations in Myasthenia Gravis. MEEI.
2. Jan. 24, 1989 Alcohol Withdrawal in the Perioperative Period. MEEI.
3. Mar. 30, 1989 Cardiac Output Computer and Invasive Monitoring Equipment. In-service, MEEI.

4. Mar. 31, 1989 Upcoming Trial at MEEI - Patient Controlled Analgesia: Toward More Effective Analgesia. Department of Nursing, MEEI.
5. May 25, 1989 Patient Controlled Analgesia: Pharmacokinetics and Pharmacodynamics. Otolaryngology Grand Rounds, MEEI.
6. Apr. 5, 1990 Respiratory Care of the ENT Patient. Otolaryngology Grand Rounds, MEEI.
7. Nov. 26, 1990 Chronic Cancer Pain Management. Nursing Grand Rounds, MEEI.
8. Mar. 6, 1991 Anesthetic and Surgical Considerations for Malignant Hyperthermia. Department of Ophthalmology, MEEI.
9. Oct. 27, 1994 Managing Chronic Pain: Case Examples of Treatment for Chronic and Neuropathic Pain of the Head, Neck, and Eyes in a Multidisciplinary Approach. Combined Grand Rounds, sponsored by the Department of Social Work, 1994 Madeline Shipsey Lecture, MEEI.
10. Feb. 6, 1995 Pain Management in Head and Neck Cancer Patients. Basic Sciences Course for ENT Residents of MEEI. Chairman, ENT, Dr. J. Nadol. Course Coordinator: Andrea Zweibel, ENT Education Office, MEEI.
11. May 11, 1995 Nursing Grand Rounds. 'A Collaborative Approach to a Patient with a Failed Skin Graft.' Nursing Dept., MEEI. Coordinator: Ann Shelley, RN.
12. Feb. 8, 1996 Pain Management in Head and Neck Cancer Patients. Basic Sciences Course for ENT Residents of MEEI. Chairman, ENT, Dr. J. Nadol. Course Coordinator: Andrea Zweibel, ENT Education Office, MEEI.
13. Feb. 8, 1996 Management of Paranasal Sinus Pain and Headache. Clinical Pathology Conference, Dept. of Otolaryngology, MEEI. Director, Dr. Salah Salman.
14. Feb. 6, 1997 Pain Management in Head and Neck Cancer Patients. Basic Sciences Course for ENT Residents of MEEI. Chairman, ENT, Dr. J. Nadol. Course Coordinator: Andrea Zweibel, ENT Education Office, MEEI.
15. June 4, 1997 Modern Approaches to Chronic Pain Management. Annual Spring Meeting, MEEI. Board of Trustees and Office of the President.
16. Dec. 18, 1997 Pain Management in Head and Neck Cancer Patients. Basic Sciences Course for ENT Residents of MEEI. Chairman, ENT, Dr. J. Nadol. Course Coordinator: Andrea Zweibel, ENT Education Office, MEEI.
17. Sept. 11, 1998 Current Pain Topics, and Latest Treatments. Leadership Group, MEEI. President, Curt Smith.
18. Mar. 18, 1999 Pain Management in Head and Neck Cancer Patients. Basic Sciences Course for ENT Residents of MEEI. Chairman, ENT, Dr. J. Nadol. Course Coordinator: Andrea Zweibel, ENT Education Office, MEEI.
19. Feb. 8, 2000 Concepts in Pain Management. MGH Pediatric Anesthesia and Surgical Lecture Series.

Dr. Eric Shank, Coordinator.

20. Jan. 18, 2001 Review of Current Concepts in Pain Management. MEEI Dept. of Otolaryngology Grand Rounds. Gregory Randolph, MD, Coordinator.

21. May 6, 2002 Botulinum Toxin and Facial Pain: Open Label Study. Chronic Pain Rounds, Mass. General Hospital.

Other Experience:

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| 1973 | Directed and hosted a radio program segment for a series called 'Multiversity' on WBUR, FM Radio Boston, Massachusetts |
| 1968-1983 | Star Market Company, Cambridge, Massachusetts
Part time - Responsibilities included preparation of perishable and non-perishable foods; preparation of meats, produce and seafood; preparation of payroll, accounting; and management of various departments, including service personnel while attending secondary, college, dental, and medical schools. |
| 1980-Present | Dentistry, both direct patient care and consultations. |
| 1993 | Reviewer, Anesthesiology |
| 1993 | Reviewer, Journal of Clinical Anesthesia. |
| 1993-1997 | Associate Editor, The Phi Delta Epsilon News and Scientific Journal.
Publication Office: 1898 East Southern Ave., Tempe, AZ 85282 |
| 1995-1997 | Treasurer, The Foundation of the Phi Delta Epsilon Medical Fraternity.
1898 East Southern Ave., Tempe, AZ 85282 |

Bibliography

Original Reports:

1. Jones II GJ, Acquadro MA, Carmody MA. Long-chain enals via carbonyl-olefin metathesis. An application in pheromone synthesis. Journal of the Chemical Society, Chemical Communications, 1975; 6:206-207.
2. Acquadro MA, Riley TL. Reappraisal of radionuclide cisternograms and the question of normal pressure hydrocephalus: A review of clinical practice. Journal of Clinical and Experimental Gerontology 1987; 9(2):121-130.
3. Acquadro MA, Borodic GE. Treatment of myofascial pain with botulinum A toxin. Anesthesiology 1994; 80:705-706.
4. Pedrosa CA, Ahern DK, McKenna MJ, Ojemann RG, Acquadro MA. Determinants and impact of headache after acoustic neuroma surgery. The American Journal of Otology 1994; 15:793-797.

5. Ward JB, Niffenegger AS, Lavin CW, Acquadro MA, Ahern DK, Smith PV, McKeown CA. The use of propofol and mivacurium anesthetic technique for the immediate post-operative adjustment of sutures in strabismus surgery. *Ophthalmology* 1995; 102:122-128.
6. Acquadro MA, Nghiem TX, Beach TB, Ahern DK, Donlon Jr. JV, Joseph MP. Acquired QT interval changes and neck dissections. *J Clin Anesth* 1995; 7:54-57.
7. Abdi S, Acquadro MA. Technical failure of desflurane vaporizer tec-6. *Anesthesiology* 1995; 83:226-227.
8. Rubin AD, Chen VN, Acquadro MA. Cluster headache presenting with orbital inflammation. *Ophthalmic Surgery and Lasers* 1996; 27:143-146.
9. Acquadro MA, Montgomery WW. Treatment of chronic paranasal sinus pain with minimal sinus pathology. *Ann Otol Rhinol Laryngol* 1996; 105:607-614.
10. Acquadro MA, Joseph MJ, Salman SD. An analysis of pain and endoscopic sinus surgery for sinusitis. *Ann Otol Rhinol Laryngol* 1997; 106:305-309.
11. Acquadro MA. Headache and sinusitis. *Curr Opin Otol & Head and Neck Surg* 1998; 6:2-5.
12. Borodic G, Acquadro M, Johnson E. Botulinum toxin therapy, composition, and tissue mechanisms. *Expert Opinions on Investigational Drugs* 10:1531-1544, 2001.
13. Borodic GE, Acquadro MA. The use of botulinum toxin for the treatment of chronic facial pain. *The Journal of Pain* Vol 3, no 1, pp 21-27, 2002.

Abstracts:

1. Borodic G, Acquadro M. Management of facial pain with botulinum toxin in a tertiary pain clinic. *Archives of Pharmacology, Supplement 2 to volume 365, # 22, page R 14: June 2002.*

Case Discussion:

1. Acquadro MA (discussant): Rubin P, et al. Case Records of the Massachusetts General Hospital (case 4-1993). *New England Journal of Medicine* 1993; 328:266-275.

Reviews and Educationally Relevant Publications

Chapters:

1. Acquadro MA. Recovery Room Care and Problems Following Ophthalmic and Otolaryngologic Surgery. In: McGoldrick KE (ed). *Anesthesia for Ophthalmic and Otolaryngologic Surgery*. Philadelphia: WB Saunders, 1992:291-302.

2. Acquadro MA. Anesthesia for Head and Neck Surgery. In: Davison JK, Eckhardt WF, Perese DA (eds). Clinical Anesthesia Procedures of the Massachusetts General Hospital, 4th ed. Little Brown, Boston, 1993:390-401.
3. Acquadro MA, Kim JC, Kini MM. Anesthetics. In: Albert DM, Jakobiec FA (eds). Principles and Practice of Ophthalmology, Basic Sciences. WB Saunders, Philadelphia, 1993:929-940.
4. Acquadro MA. Anesthetic and Perianesthetic Medications. In: Zimmerman TJ, Kooner KS, Sharir M, Fechtner RD (eds). Textbook of Ocular Pharmacology. Raven Press, New York, 1997:764-770.
5. Acquadro MA. Anesthetic Considerations for Ophthalmic Surgery. In: Zimmerman TJ, Kooner KS, Sharir M, Fechtner RD (eds). Textbook of Ocular Pharmacology. Raven Press, New York, 1997:771-780.
6. Lydon A, Acquadro MA. Facial Pain. In: Ballantyne J (ed). The Massachusetts General Hospital Handbook of Pain Management, 2nd ed. Lippincott Williams and Wilkins, Philadelphia, 2002: 411-427.
7. Lydon A, Acquadro MA. Anesthesia for Head and Neck Surgery. In: Clinical Anesthesia Procedures of the Massachusetts General Hospital. In press.

Course Syllabi:

1. Approach to Comprehensive Pain Management for ENT and Eye Patients. For: Harvard Continuing Medical Education Course, Anesthetic Management for Otorhinolaryngologic and Ophthalmic Surgery. October, 1991.
2. Paranasal Sinus, Head, and Facial Pain. For: Harvard Continuing Medical Education Course, Sinus and Trans-Sinus Surgery: Traditional and Endoscopic. April, 1994.
3. Orofacial Pain. For: American Academy of Pain Medicine, 1995 Review Course in Pain Medicine, February, 1995.
4. Selected Topics in Anesthesia for Ophthalmic Surgery. For: Harvard Continuing Medical Education Course, Intensive Review of Ophthalmology, updated - 1992, 1993, 1994, & 1995.

Other Articles:

1. Acquadro MA: Comprehensive Approach to Pain in Spasmodic Torticollis. National Spasmodic Torticollis Association Newsletter 1994; 11:4.
2. Acquadro MA: Overview of Pain Therapy. Phi Delta Epsilon News and Scientific Journal 1994; 85(2):10-13.

Presentations at Meetings:

1. McKeown CA, Lavin CW, Acquadro MA, et al: The Use of Propofol and Mivacurium Anesthetic Technique for the Immediate Postoperative Adjustment of Sutures. Poster Session, American

Association for Pediatric Ophthalmology and Strabismus. Annual Meeting, Palm Springs, CA, April 17-21, 1993.

2. Ward JB, McKeown CA, Niffenegger AS, et al: The Use of Propofol and Mivacurium Anesthetic Technique for the Immediate Postoperative Adjustment of Sutures in Strabismus Surgery. Poster Session, American Academy of Ophthalmology, Annual Meeting, Chicago, IL, November 13-17, 1993.
3. McKeown CA, Ward JB, Niffenegger AS, et al: The Use of Propofol and Mivacurium Anesthetic Technique for the Immediate Postoperative Adjustment of Sutures in Strabismus Surgery. Poster Session, Association for Research in Vision and Ophthalmology, Annual Meeting, Sarasota, FL, April 30 - May 6, 1994.
4. Niffenegger AS, Ward JB, Lavin CW, et al: Low Incidence of Nausea and Vomiting Following General Anesthesia for Adult Strabismus Surgery Employing Continuous Infusions of Propofol, Mivacurium, and Alfentanil. Poster Session, Association for Research in Vision and Ophthalmology, Annual Meeting, Sarasota, FL, April 30 - May 6, 1994.
5. Borodic GE, Acquadro MA. Experience in Utilization of Botulinum Toxin for the Treatment of Head and Neck Pain Disorders. International Conference on Toxins. Orlando, Florida, November 20-23, 1999.
6. Borodic GE, Acquadro MA. Botulinum Toxin for Human Headache Disorders. New England Ophthalmology Society, Boston, MA, June 2, 2000.
7. Borodic GE, Acquadro MA. Botulinum Toxin for Chronic Facial Pain. New England Ophthalmology Society, Boston, MA, June 19, 2001.
8. Application of botulinum toxin in multiple pain syndromes of the head and neck region. International Conference 2002: Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hanover, Germany, June 8 - 11, 2002, Hans Bigalke, Course Coordinator.
9. Sensory nerve adaptation, pain management, and application of botulinum toxin in a tertiary care pain center. International Conference 2002: Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hanover, Germany, June 8 - 11, 2002, Hans Bigalke, Course Coordinator.
10. Borodic GE, Acquadro MA. Botulinum Toxin for Chronic Facial Pain - Update. New England Ophthalmology Society, Boston, MA, November 15, 2003.